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ORIGINAL RESEARCH

Laboratory Biomarker Profiles and Phenotypic Discrimination in Coronary Artery Disease with Metabolic and Renal Comorbidities: A Cross-Sectional Study

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Background: Coronary artery disease (CAD) frequently coexists with metabolic and renal comorbidities, including type 2 diabetes mellitus (T2DM), hyperuricemia (HUA), and chronic kidney disease (CKD), which may influence laboratory biomarker profiles. This study aimed to characterize haematological, biochemical, and urinary parameters across CAD phenotypes and identify laboratory predictors associated with these comorbidity patterns.

Methods: A retrospective cross-sectional study was conducted at Guangzhou Liwan Central Hospital between January 1 and December 31, 2024, including 544 adult patients with CAD. Diagnoses of CAD, T2DM, HUA, and CKD were defined according to established clinical criteria documented in hospital electronic medical records. Patients were stratified into seven phenotypic subgroups based on the presence of T2DM, HUA, and CKD. Demographic characteristics and laboratory parameters—including haematological indices, biochemical markers, and urinary findings—were extracted from electronic records. Between-group comparisons were performed using ANOVA and chi-square tests, and multivariable logistic regression was used to identify laboratory predictors associated with CAD comorbidity phenotypes.

Results: Significant differences in demographic and laboratory parameters were observed across CAD phenotypes. Gender distribution differed significantly between groups ($p = 0.004$). The CAD+HUA group had the highest mean age (84.7 ± 10.1 years), whereas the CAD+T2DM+CKD group had the lowest (76.4 ± 11.0 years; $p = 1.77 \times 10^{-7}$). Multivariable logistic regression identified leukocyte esterase positivity (OR 2.41, 95% CI 1.38–4.19), β2-microglobulin (OR 1.52, 95% CI 1.16–2.01), potassium (OR 1.37, 95% CI 1.08–1.74), glucosuria (OR 0.58, 95% CI 0.35–0.96), nitrite positivity (OR 1.89, 95% CI 1.07–3.34), and serum calcium (OR 0.73, 95% CI 0.55–0.96) as significant predictors of CAD comorbidity phenotypes.

Conclusion: Haematological, biochemical, and urinary biomarkers differ across CAD phenotypes with metabolic and renal comorbidities. These laboratory indicators show moderate discriminatory potential for identifying CAD comorbidity patterns, although further validation in larger prospective cohorts is required.

Keywords: coronary artery disease, comorbidities, biomarkers, logistic regression, risk stratification

Introduction

Cardiovascular diseases (CVDs) currently represent the leading cause of death worldwide, responsible for approximately 19.8 million deaths in 2022, accounting for ~32% of all global mortality.[1,2] Among these, ischemic heart disease (including coronary artery disease, CAD) ranks as the primary contributor to cardiovascular burden.[3] In recent decades, absolute numbers of CVD deaths have risen (from ~12.4 million in 1990 to ~19.8 million in 2022), largely due to population growth and aging, although age-standardized mortality rates have declined in many regions.[4] CAD remains

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a major public health challenge. In 2022, an estimated 315 million individuals globally were living with CAD, with an age-standardized prevalence of 3605 per 100,000 (95% uncertainty interval 2892–4454), representing an ~18% decline from 1990 estimates.[5] Despite such trends, CAD still accounts for approximately 15.5% of all global deaths.[6] In general populations, cardiovascular risk models like the Framingham Risk Score and SCORE2 yield discrimination metrics (C-statistics) in the range 0.70 to 0.80.[7] However, their performance weakens in individuals with comorbid conditions (type 2 diabetes mellitus [T2DM], hyperuricemia [HUA], chronic kidney disease [CKD]), where biomarker behaviour and pathophysiology deviate from "average" profiles.[8] Hyperuricemia has been increasingly recognized as an independent risk factor for cardiovascular events. In a pooled meta-analysis of 32 cohort studies (1,134,073 participants), elevated serum uric acid was associated with a 45% increased risk of cardiovascular disease (CVD) mortality (hazard ratio [HR] 1.45, 95% confidence interval [CI] 1.33–1.58).[9] The association showed nonlinearity, with risks rising more steeply beyond ~6 mg/dL. Patients with CKD often display altered elimination kinetics and accumulation of metabolites, complicating the interpretation of circulating biomarker levels.[10] Several haematological and biochemical parameters have individually been linked to CAD incidence, progression, or prognosis: leukocyte count, neutrophil–lymphocyte ratio, platelet count, liver enzymes, albumin, electrolytes, and β_2-macroglobulin, among others.[11] Urine provides a complementary and non-invasive substrate for biomarker analysis, reflecting renal–cardiovascular interrelationships, filtration processes, and early molecular perturbations. Recent studies have highlighted the relevance of urinary biomarkers in cardiovascular disease. Urinary components reflecting renal dysfunction, endothelial injury, and inflammatory processes have been associated with increased cardiovascular risk and adverse outcomes. These findings support the use of urinary markers as accessible and non-invasive indicators that complement traditional cardiovascular risk factors in disease prediction and monitoring.[12,13] Urinary proteomic classifiers have been developed for CAD risk prediction: for example, Wei et al derived a 160-peptide urinary signature yielding an area under the ROC curve (AUC) of 0.82 (95% CI 0.78–0.87) over an 8-year prediction interval, outperforming prior signatures (eg. CAD238: AUC 0.71, 95% CI 0.66–0.77; ACSP75: AUC 0.53, 95% CI 0.47–0.60).[14] In multivariable Cox models, each 1-SD increment in the classifier corresponded to HR 1.54 (95% CI 1.26–1.89, $p < 0.0001$).[8] Earlier validation in the ASCOT cohort (n = 60) showed that the CAD238 urinary panel predicted incident CAD independently of age and sex ($p = 0.021$ via survival analysis).[15] Nevertheless, prior studies often focus on either urinary biomarkers or plasma/serum biomarkers in isolation. Few have integrated haematological, biochemical, and urinary markers in a unified predictive framework to discriminate among CAD phenotypes stratified by comorbidity burden (eg, CAD + T2DM + CKD; CAD + HUA). Given these considerations, the present study aimed to comprehensively characterize laboratory biomarker profiles across CAD phenotypes defined by common metabolic and renal comorbidities, including T2DM, HUA, and CKD. By integrating routine haematological indices, biochemical parameters, and urinary test results, we sought to identify laboratory markers associated with distinct CAD comorbidity patterns. Multivariable logistic regression analysis was applied to quantify these associations using odds ratios with 95% confidence intervals. Rather than developing a clinical prediction tool or directly comparing performance with established cardiovascular risk scores, this study focuses on exploring how routinely measured laboratory indicators may collectively reflect the heterogeneity of CAD in the presence of metabolic and renal comorbidities and potentially inform future risk stratification and mechanistic investigations.

Methods

The present study was conducted in accordance with the Helsinki Declaration guidelines. As this was a retrospective study, the requirement for informed patient consent was waived by the Institutional Ethical Committee of Guangzhou Liwan Central Hospital, Guangzhou. The study was approved by the same committee, under approval letter number 2025024.

Study Design and Population

This retrospective single-centre observational study was conducted at Guangzhou Liwan Central Hospital, Guangzhou, China. The study included all consecutive adult patients diagnosed with coronary artery disease (CAD) between January 1, 2024 and December 31, 2024 who met the inclusion criteria and had complete laboratory data available in the hospital electronic medical record. The study population included adult patients, both male and female, who were

diagnosed with CAD based on clinical evaluation, imaging, and laboratory investigations performed during routine inpatient or outpatient visits. Eligible patients were required to be aged 18 years or older at the time of diagnosis, have a confirmed diagnosis of CAD established through clinical history, electrocardiography, cardiac biomarkers, or coronary angiography, and have complete haematological, biochemical, and urinary laboratory data recorded at the time of CAD diagnosis or follow-up. CAD was diagnosed according to established clinical guidelines and confirmed by at least one of the following criteria: (1) documented coronary artery stenosis ≥50% in at least one major epicardial coronary artery as demonstrated by coronary angiography or coronary computed tomography angiography (CCTA); (2) a documented history of myocardial infarction or prior coronary revascularization, including percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG); or (3) clinical symptoms consistent with myocardial ischemia accompanied by electrocardiographic changes or elevated cardiac biomarkers (eg, cardiac troponin) consistent with ischemic heart disease.Type 2 diabetes mellitus (T2DM) was defined according to the diagnostic criteria of the American Diabetes Association, including fasting plasma glucose ≥7.0 mmol/L (126 mg/dL), glycated hemoglobin (HbA1c) ≥6.5%, 2-hour plasma glucose ≥11.1 mmol/L during an oral glucose tolerance test, or a documented clinical diagnosis of diabetes with ongoing antidiabetic treatment. Hyperuricemia (HUA) was defined as a serum uric acid level >420 μmol/L (7.0 mg/dL) in men or >360 μmol/L (6.0 mg/dL) in women, or a documented clinical diagnosis of hyperuricemia or treatment with urate-lowering therapy. Chronic kidney disease (CKD) was defined according to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 persisting for at least three months or evidence of kidney damage, including persistent proteinuria or structural abnormalities documented in medical records. Patients were excluded if they had acute infectious diseases, autoimmune disorders, malignancies, or haematological diseases that could confound biomarker profiles; if they were pregnant or lactating; if they were receiving immunosuppressive or cytotoxic therapy; if medical records were incomplete or key laboratory parameters were missing; or if they had experienced acute coronary syndromes within 30 days prior to sample collection to avoid acute-phase confounding effects. Eligible patients were stratified into eight clinical subgroups based on the presence of metabolic and renal comorbidities: CAD only, CAD + T2DM, CAD + HUA, CAD + CKD, CAD + T2DM + HUA, CAD + HUA + CKD, CAD + T2DM + CKD, and CAD + T2DM + HUA + CKD. This stratification allowed for comparative evaluation of haematological, biochemical, and urinary parameters across clinically distinct CAD phenotypes with differing comorbidity burdens.

Data Collection

Electronic medical records were systematically retrieved from the Hospital Records Department of Guangzhou Liwan Central Hospital. All patient information was de-identified in accordance with institutional ethical guidelines. Demographic data, including age and sex, as well as comorbidities such as type 2 diabetes mellitus (T2DM), chronic kidney disease (CKD), and hyperuricemia (HUA), were collected. Haematological parameters included complete blood counts (white blood cell [WBC] count, red blood cell [RBC] count, haemoglobin [Hb], haematocrit [HCT], platelet count [PLT]), platelet indices (mean platelet volume, platelet distribution width), and differential leukocyte counts (neutrophils, lymphocytes, monocytes, eosinophils, and basophils). Inflammatory markers, specifically C-reactive protein (CRP), were also recorded. Biochemical parameters encompassed liver function tests (alanine aminotransferase [ALT], total protein [TP], albumin [ALB], globulin [GLB]), renal function markers (creatinine [CREA], β2-microglobulin [BMG], uric acid [UA]), and electrolytes (sodium [Na^+], potassium [K^+], chloride [Cl^-], calcium [Ca^{2+}]). Urine analysis results, obtained from dipstick testing, included leukocyte esterase (LEU), protein (PRO), glucose (GLU), occult blood (BLD), nitrite (NIT), specific gravity (SG), and pH. All laboratory measurements were performed in the hospital's accredited clinical laboratory following standard quality control procedures. All laboratory data were collected from routine tests performed at patient admission or follow-up visits.

Statistical Analysis

Continuous variables were summarized as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Comparisons between patient subgroups were conducted using one-way analysis of variance (ANOVA) for normally distributed continuous variables and Chi-square tests for categorical variables. To

assess the association between laboratory parameters and specific disease phenotypes, including CAD combined with T2DM, CKD, HUA, or their combinations, multivariate binary logistic regression analyses were performed. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Variables for regression modeling were selected based on clinical relevance and univariate statistical significance. Multicollinearity among candidate predictors was assessed using variance inflation factor (VIF) analysis, and highly correlated variables were not included simultaneously in the regression models. In addition, a sensitivity analysis excluding the smallest subgroup (CAD + T2DM + CKD) was conducted to evaluate the robustness of the findings. All statistical analyses were conducted using standard statistical software, and a two-tailed p-value < 0.05 was considered statistically significant, with notations as follows: $p < 0.05$, $p < 0.01$, $p < 0.001$, and $p < 0.0001$.

Results

Patient Characteristics

A total of 544 patients were included and distributed across seven clinical subgroups. The CAD+T2DM group comprised 157 patients, including 44 males (28.0%) and 113 females (72.0%). The CAD+HUA group included 156 patients, with 71 males (45.5%) and 85 females (54.5%). The CAD+CKD group included 74 patients, consisting of 17 males (23.0%) and 57 females (77.0%). Other subgroups included CAD+T2DM+HUA (60 patients; 23 males [38.3%], 37 females [61.7%]), CAD+HUA+CKD (54 patients; 15 males [27.8%], 39 females [72.2%]), CAD+T2DM+CKD (17 patients; 8 males [47.1%], 9 females [52.9%]), and CAD+T2DM+HUA+CKD (26 patients; 7 males [26.9%], 19 females [73.1%]). Gender distribution differed significantly across subgroups (p = 0.004). The mean age was highest in the CAD+HUA group (84.7 ± 10.1 years) and lowest in the CAD+T2DM+CKD group (76.4 ± 11.0 years), with significant differences among subgroups ($p = 1.77 \times 10^{-7}$) Table 1.

Hematological and Biochemical Profiles

Serum ALT levels were highest in CAD+CKD (24.45 ± 26.96 U/L) and lowest in CAD+T2DM+HUA (13.80 ± 12.99 U/L; $p = 0.036$). Total protein (TP), albumin (ALB), and globulin (GLB) concentrations differed significantly across subgroups (TP: 61.23–66.09 g/dL, $p = 0.0003$; ALB: 33.00–37.99 g/dL, $p = 0.005$; GLB: 26.18–31.17 g/dL, p = 0.0002). Electrolytes including calcium (Ca: 2.21–2.33 mg/dL; $p = 0.025$), sodium (Na: 137.56–139.49 mg/dL; $p = 0.0005$), chloride (Cl: 101.54–103.87 mg/dL; $p = 0.0009$), and potassium (K: 3.90–4.42 mg/dL; $p = 0.0002$) also varied significantly. Electrolytes including calcium (2.21–2.33 mmol/L; $p = 0.025$), sodium (137.56–139.49 mmol/L; p = 0.0005), chloride (101.54–103.87 mmol/L; $p = 0.0009$), and potassium (3.90–4.42 mmol/L; $p = 0.0002$) also varied significantly across subgroups. β2-microglobulin (BMG) levels were elevated in patients with combined metabolic comorbidities, reaching 5.31 ± 2.52 mg/L in CAD+T2DM+HUA ($p<0.0001$) (Figure 1). Additional markers including CRP, AST, PAB, and TBIL did not differ significantly among groups.

Urinary Parameters

Urine analyses revealed significant differences in specific gravity (SG: 1.01–1.02; $p = 0.045$) and pH (5.58–6.26; $p=0.0026$). Positive leukocyte esterase (LEU) was most frequent in CAD+HUA+CKD (42/12; 77.8%) and CAD+CKD (42/32; 56.8%), compared to CAD+T2DM (53/104; 33.8%; $p<0.0001$). Proteinuria (PRO), glucosuria (GLU), haematuria (BLD), and nitrite positivity (NIT) also showed significant differences (all p < 0.001). Renal function markers including urea (6.73–11.10 mmol/L; $p = 0.0026$), creatinine (83.93–153.97 μmol/L; $p < 0.0001$), and uric acid (298.42–452.91-μmol/L; $p < 0.0001$) were elevated in patients with combined metabolic and renal comorbidities (Figure 1).

Logistic Regression Modelling

Multivariate logistic regression identified key predictors for combined disease phenotypes. For CAD+HUA+CKD, significant predictors included positive leukocyte esterase (OR = 6.97, 95% CI 2.61–18.59), elevated β2-microglobulin (OR = 1.35, 95% CI 1.07–1.71), and serum potassium (OR = 1.69, 95% CI 0.76–3.74). In contrast, glucosuria was inversely associated with CAD+T2DM+HUA (OR = 0.21, 95% CI 0.09–0.48), while nitrite positivity strongly predicted

Table 1 Demographic Characteristics and Laboratory Parameters of Study Participants Across Clinical Groups

	CAD+T2DM	CAD+HUA	CAD+CKD	CAD+T2DM+HUA	CAD+HUA+CKD	CAD+T2DM+CKD	CAD+T2DM+HUA+CKD	Method	*P* value
Total Number	157	156	74	60	54	17	26	Chi.Square	2.2E-16****
Age (Mean ± SD)	77.55 ± 9.40	75.97 ± 11.44	84.72 ± 10.07	75.18 ± 10.79	78.96 ± 8.85	80.76 ± 13.14	76.38 ± 11.00	ANOVA	1.77e-07****
Gender (Male/Female)	44/113	71/85	17/57	23/37	15/39	8/9	7/19	Chi.Square	0.00412**
Blood Test									
WBC (10^9/L)	7.80 ± 2.82	7.62 ± 2.97	7.25 ± 3.41	8.31 ± 2.90	8.93 ± 4.09	7.94 ± 2.16	7.26 ± 2.24	ANOVA	0.0471*
RBC (10^9/L)	3.82 ± 0.89	4.10 ± 0.97	3.39 ± 0.90	4.34 ± 0.94	3.75 ± 1.07	3.79 ± 0.56	3.99 ± 0.95	ANOVA	8.87E-08***
PLT (10^9/L)	242.30 ± 66.07	241.24 ± 87.46	228.80 ± 78.04	243.83 ± 74.81	258.04 ± 84.30	215.82 ± 65.07	199.23 ± 71.42	ANOVA	0.0356*
Lym (10^9/L)	1.63 ± 0.67	1.63 ± 0.95	1.51 ± 0.97	1.74 ± 0.61	1.54 ± 0.68	1.33 ± 0.73	1.43 ± 0.62	ANOVA	0.344
Mon (10^9/L)	0.65 ± 0.20	0.67 ± 0.44	0.62 ± 0.33	0.66 ± 0.23	0.64 ± 0.28	0.72 ± 0.29	0.65 ± 0.17	ANOVA	0.914
Neu (10^9/L)	5.37 ± 3.11	5.07 ± 2.50	4.81 ± 2.64	5.70 ± 2.87	6.31 ± 3.97	5.75 ± 1.86	4.90 ± 1.98	ANOVA	0.0701
Eos (10^9/L)	0.20 ± 0.15	0.22 ± 0.23	0.25 ± 0.32	0.18 ± 0.13	0.32 ± 0.25	0.12 ± 0.11	0.22 ± 0.21	ANOVA	0.00416**
Bas (10^9/L)	0.033 ± 0.017	0.033 ± 0.018	0.031 ± 0.020	0.033 ± 0.025	0.034 ± 0.020	0.026 ± 0.017	0.037 ± 0.027	ANOVA	0.716
NRBC (10^9/L)	0.0036 ± 0.026	0.0047 ± 0.022	0.0015 ± 0.0052	0.0013 ± 0.0047	0.0011 ± 0.0037	0.00059 ± 0.0024	0.00038 ± 0.0020	ANOVA	0.709
MPV (fL)	9.57 ± 0.72	9.84 ± 0.92	9.69 ± 0.86	9.66 ± 1.12	9.70 ± 0.87	9.95 ± 1.01	10.04 ± 0.89	ANOVA	0.256
PDW (fL)	10.33 ± 1.73	10.52 ± 1.88	10.12 ± 1.99	10.49 ± 2.50	10.37 ± 1.94	10.55 ± 2.02	11.22 ± 1.82	ANOVA	0.318
RDW-SD (fL)	46.44 ± 7.28	45.71 ± 7.27	48.97 ± 5.98	45.32 ± 6.64	47.05 ± 5.64	44.58 ± 3.65	45.17 ± 2.88	ANOVA	0.0103*
MCV (fL)	91.27 ± 8.76	87.98 ± 11.30	92.96 ± 10.06	86.11 ± 11.71	88.48 ± 11.92	89.46 ± 6.22	87.46 ± 8.44	ANOVA	0.000519***
CRP (mg/L)	16.91 ± 26.94	17.48 ± 31.79	23.06 ± 37.30	16.87 ± 30.65	21.21 ± 32.13	18.23 ± 22.35	9.96 ± 14.89	ANOVA	0.611
ALT (U/L)	18.48 ± 22.85	18.43 ± 13.68	15.62 ± 8.76	24.45 ± 26.96	13.80 ± 12.99	19.35 ± 9.74	14.27 ± 6.10	ANOVA	0.0356*
AST (U/L)	22.55 ± 14.33	21.47 ± 19.59	24.88 ± 16.09	27.82 ± 39.51	20.54 ± 15.15	20.06 ± 4.92	15.88 ± 4.83	ANOVA	0.161
TP (g/dL)	66.00 ± 6.53	62.26 ± 11.40	62.47 ± 8.02	65.30 ± 5.07	65.18 ± 5.18	66.09 ± 4.17	61.23 ± 7.32	ANOVA	0.000328***
ALB (g/dL)	35.77 ± 6.31	35.26 ± 5.93	33.00 ± 5.02	35.88 ± 4.36	34.43 ± 5.05	37.99 ± 4.23	35.29 ± 6.40	ANOVA	0.00525**
GLB (g/dL)	30.30 ± 4.65	29.32 ± 5.11	31.17 ± 6.68	29.63 ± 4.27	30.84 ± 5.29	27.65 ± 3.70	26.18 ± 4.71	ANOVA	0.000225***
TBIL (umol/L)	8.73 ± 3.99	9.84 ± 6.12	8.26 ± 4.28	9.45 ± 4.35	8.27 ± 7.27	8.77 ± 2.80	7.90 ± 4.52	ANOVA	0.181
DBIL (umol/L)	2.31 ± 2.03	2.65 ± 3.39	2.40 ± 1.99	2.93 ± 3.28	2.76 ± 3.56	2.84 ± 1.41	2.25 ± 1.91	ANOVA	0.743
PAB (g/dL)	169.21 ± 92.35	165.95 ± 104.37	183.06 ± 90.07	160.72 ± 105.86	138.29 ± 110.41	192.38 ± 102.90	174.83 ± 122.23	ANOVA	0.254
PCT (%)	0.24 ± 0.065	0.23 ± 0.077	0.22 ± 0.070	0.24 ± 0.071	0.24 ± 0.070	0.21 ± 0.056	0.20 ± 0.067	ANOVA	0.0479*
FIB (g/L)	3.60 ± 1.19	3.54 ± 1.04	4.04 ± 1.30	4.06 ± 1.48	4.30 ± 1.50	3.57 ± 0.79	3.41 ± 1.25	ANOVA	0.000126***
Ca (mg/dL)	2.26 ± 0.13	0.23 ± 0.17	2.21 ± 0.12	2.27 ± 0.14	2.26 ± 0.15	2.33 ± 0.20	2.25 ± 0.22	ANOVA	0.0247*
Na (mg/dL)	137.56 ± 4.25	139.49 ± 4.16	139.45 ± 3.78	138.95 ± 3.01	139.13 ± 2.68	138.73 ± 3.35	139.01 ± 2.33	ANOVA	0.000502***
Cl (mg/dL)	101.54 ± 4.43	102.78 ± 4.15	103.68 ± 4.28	103.16 ± 2.91	103.44 ± 3.51	103.70 ± 3.76	103.87 ± 3.51	ANOVA	0.000887***
K (mg/dL)	3.95 ± 0.60	3.97 ± 0.50	3.90 ± 0.57	4.09 ± 0.46	4.23 ± 0.52	4.42 ± 0.42	3.96 ± 0.56	ANOVA	0.000218***
BMG (mg/L)	2.72 ± 2.24	4.24 ± 3.69	4.83 ± 2.76	3.36 ± 2.41	5.31 ± 2.52	5.27 ± 3.89	3.88 ± 1.12	ANOVA	1.12e-09****
HGB (g/L)	112.13 ± 25.53	114.81 ± 26.15	99.07 ± 23.02	118.08 ± 29.49	103.50 ± 25.39	110.53 ± 20.14	114.42 ± 26.19	ANOVA	7.320e-05***
HCT (%)	34.40 ± 7.03	35.36 ± 7.43	30.97 ± 6.43	36.85 ± 7.30	32.41 ± 7.21	33.88 ± 5.16	35.66 ± 7.90	ANOVA	2.18e-05***
MCH (pg)	29.67 ± 3.35	28.44 ± 4.42	29.51 ± 3.43	27.60 ± 4.99	28.23 ± 4.32	29.12 ± 2.99	28.27 ± 3.94	ANOVA	0.00675**
MCHC (g/L)	324.22 ± 14.10	322.98 ± 15.25	317.43 ± 15.28	319.60 ± 20.80	318.63 ± 14.78	325.24 ± 16.17	318.19 ± 15.88	ANOVA	0.0153*
RDW-CV (%)	14.14 ± 2.35	14.67 ± 2.96	14.62 ± 1.97	14.89 ± 2.78	15.02 ± 2.26	13.75 ± 1.50	14.21 ± 1.68	ANOVA	0.133

(*Continued*)

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Table 1 (Continued).

	CAD+T2DM	CAD+HUA	CAD+CKD	CAD+T2DM+HUA	CAD+HUA+CKD	CAD+T2DM+CKD	CAD+T2DM+HUA+CKD	Method	*P* value
Urine Test									
SG	1.01 ± 0.0075	1.01 ± 0.0061	1.01 ± 0.0062	1.02 ± 0.0090	1.01 ± 0.0071	1.01 ± 0.0059	1.01 ± 0.0053	ANOVA	0.0452*
PH	6.16 ± 0.96	6.00 ± 0.75	6.12 ± 1.07	5.83 ± 0.69	6.26 ± 0.90	5.74 ± 0.53	5.58 ± 0.59	ANOVA	0.00262**
LEU (pos/neg)	53/104	25/131	42/32	18/42	42/12	5/12	7/19	Chi.Square	3.432e-16****
PRO (pos/neg)	17/140	17/139	23/51	16/44	13/41	2/15	15/7	Chi.Square	8.424e-11****
GLU (pos/neg)	53/104	17/139	8/66	18/42	6/48	5/12	22/4	Chi.Square	2.2E-16****
KET (pos/neg)	5/152	1/155	1/73	1/59	0/54	0/17	0/26	Chi.Square	0.494
URO (pos/neg)	4/153	1/155	1/73	1/59	1/53	0/17	0/26	Chi.Square	0.8434
BIL (pos/neg)	0/157	0/156	0/74	1/59	0/54	0/17	0/26	Chi.Square	0.2322
Urea (μmol/L)	6.73 ± 5.09	8.87 ± 7.19	9.88 ± 5.84	9.88 ± 11.14	9.56 ± 4.07	11.10 ± 6.61	8.40 ± 2.78	ANOVA	0.00262**
CREA (μmol/L)	83.93 ± 54.39	114.05 ± 73.65	145.48 ± 63.24	117.74 ± 84.72	127.24 ± 41.87	153.97 ± 89.89	136.81 ± 40.78	ANOVA	5.72e-11***
UA (μmol/L)	298.42 ± 98.11	458.88 ± 143.18	362.03 ± 114.28	436.60 ± 108.32	452.91 ± 123.81	400.65 ± 103.77	446.62 ± 95.40	ANOVA	2e-16****
BLD (pos/neg)	49/108	62/94	20/54	9/51	18/36	2/15	2/24	ANOVA	0.000755***
NIT (pos/neg)	27/130	20/136	39/35	1/59	13/41	3/14	1/25	ANOVA	3.883e-14****

Notes: Comparisons among groups were performed using one-way ANOVA. Values are presented as mean ± SD or number. Group comparisons were performed using one-way ANOVA for continuous variables and Chi-square test for categorical variables. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$.

Abbreviations: CAD, coronary artery disease; T2DM, Type 2 diabetes mellitus; HUA, Hyperuricemia; CKD, chronic kidney disease; WBC, White blood cells; RBC, Red blood cells; Hb, Hemoglobin; PLT, Platelets; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; LDL, Low-density; lipoprotein; HDL, High-density lipoprotein; TC, Total cholesterol; TG, Triglycerides; UA, Uric acid; Cr, Creatinine.

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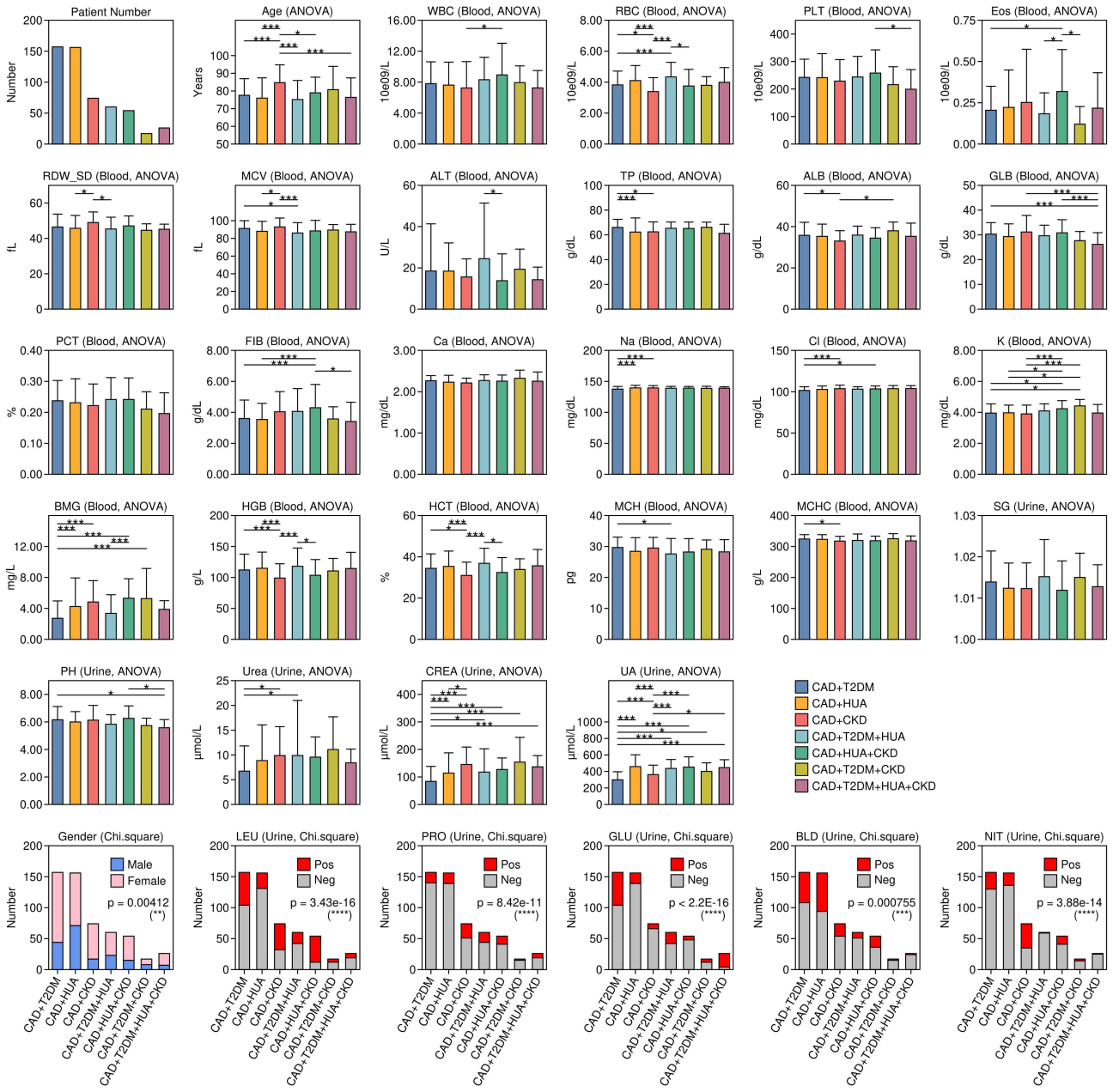

Figure 1 Comparative analysis of serum and urine biochemical parameters across CAD-associated comorbidity subgroups. Data are presented as mean ± standard deviation (SD), unless otherwise specified. Each panel illustrates a distinct hematological, biochemical, or urinary parameter measured across clinically defined subgroups, including CAD+T2DM, CAD+HUA, CAD+CKD, and their combinations. Statistical comparisons among groups were performed using one-way ANOVA for continuous variables and chi-square tests for categorical variables. Statistical significance is indicated as *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$.****$p < 0.00001$.

CAD+T2DM (OR = 11.67, 95% CI 4.10–33.25). Serum calcium emerged as a positive predictor for CAD+T2DM+CKD (OR = 6.45, 95% CI 2.70–15.4). These findings should be interpreted as exploratory associations between laboratory parameters and CAD comorbidity phenotypes rather than as validated predictive models. Logistic regression models using these features demonstrated high predictive accuracy in distinguishing disease subtypes (Figures 2). Model features and corresponding ORs with 95% CIs for all subgroups are provided in Table 2.

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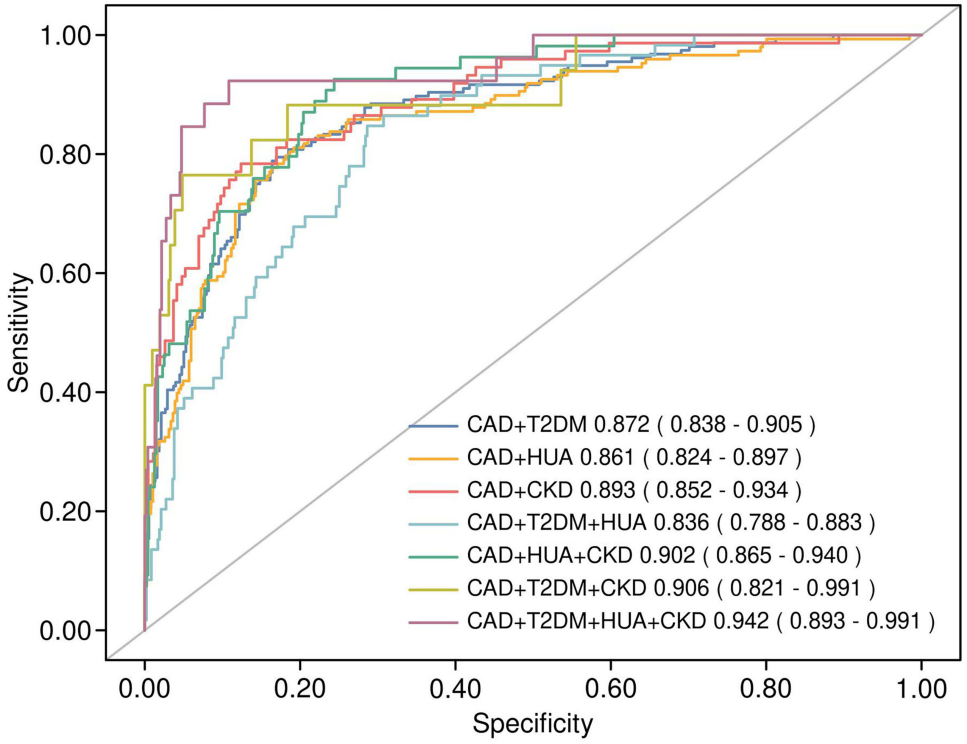

Figure 2 Predictive performance of logistic regression models (ROC curve analysis). This figure shows ROC curves for logistic regression models predicting subgroups; each line represents a model with a different combination of comorbidity groups. AUC values: AUCs in the legend indicate discrimination performance; higher AUC suggests better ability to distinguish the target subgroup from the reference. Subgroup comparisons: Models include CAD+T2DM, CAD+HUA, CAD+CKD, and combinations (eg, CAD+T2DM+HUA, CAD+HUA+CKD, CAD+T2DM+CKD, CAD+T2DM+HUA+CKD). The last line (CAD+T2DM+HUA+CKD) has the highest AUC (0.942), implying the best overall discrimination among the tested models.

Discussion

This study analysed 544 patients with coronary artery disease (CAD) and comorbidities including type 2 diabetes mellitus (T2DM), hyperuricemia (HUA), and chronic kidney disease (CKD), stratified into seven clinical subgroups. The study provides a granular view of demographic, haematological, biochemical, and urinary characteristics in these patients, offering insights into the pathophysiological interactions between CAD and its comorbid conditions. Gender distribution differed significantly among subgroups (p = 0.004). Females predominated in most groups, particularly in CAD+CKD (57/74, 77%)

Table 2 Multivariate LASSO-Penalised Logistic Regression: Predictors of CAD Comorbidity Subgroups

Predictor (Units)	**OR per Unit**	**95% CI**	***p*-value**	**Significance**	**Cohen's d vs Others**
Model 1: CAD+T2DM — n = 157 cases/544 total AIC = 474.4 BIC = 513.1 Nagelkerke R^2 = 0.435 Bootstrap AUC = 0.846 [95% CI: 0.798–0.894]					
Predictor (units)	OR per unit	95% CI	*p*-value		Cohen's d
Uric acid (μmol/L) VIF=1.3	0.99	0.99–0.99	<0.0001	****	−1.1
Glucosuria (pos vs neg) VIF=1.1	1.86	1.10–3.13	0.021	*	—
Nitrite (pos vs neg) VIF=1.1	0.57	0.31–1.07	0.08	ns	—
Creatinine (μmol/L) VIF=1.9	1	0.99–1.00	0.275	ns	−0.64
β2-Microglobulin (mg/L) VIF=1.9	0.82	0.70–0.95	0.011	*	−0.57
Total protein (g/dL) VIF=1.3	1.05	1.00–1.09	0.042	*	0.33
Sodium (mmol/L) VIF=1.1	0.91	0.86–0.97	0.004	**	−0.45
Albumin (g/dL) VIF=1.4	1.01	0.96–1.07	0.591	ns	0.15

(*Continued*)

Table 2 (Continued).

Predictor (Units)	OR per Unit	95% CI	*p*-value	Significance	Cohen's d vs Others
Model 2: CAD+HUA — n = 156 cases/544 total AIC = 502.5 BIC = 541.2 Nagelkerke R^2 = 0.379 Bootstrap AUC = 0.809 [95% CI: 0.749–0.860]					
Predictor (units)	OR per unit	95% CI	p-value		Cohen's d
Uric acid (μmol/L) VIF=1.3	1.01	1.01–1.01	<0.0001	****	0.7
Glucosuria (pos vs neg) VIF=1.0	0.31	0.17–0.57	0	***	—
Leukocyte esterase (pos vs neg) VIF=1.1	0.16	0.09–0.28	<0.0001	****	—
Creatinine (μmol/L) VIF=1.3	0.99	0.99–1.00	0	***	0.01
Proteinuria (pos vs neg) VIF=1.1	0.38	0.18–0.80	0.011	*	—
Total protein (g/dL) VIF=1.1	0.94	0.92–0.97	<0.0001	****	−0.3
Sodium (mmol/L) VIF=1.0	1.05	0.98–1.11	0.172	ns	0.26
Haematuria (pos vs neg) VIF=1.1	3.6	2.15–6.03	<0.0001	****	—
Model 3: CAD+CKD — n = 74 cases/544 total AIC = 330.8 BIC = 365.2 Nagelkerke R^2 = 0.355 Bootstrap AUC = 0.821 [95% CI: 0.735–0.890]					
Predictor (units)	OR per unit	95% CI	p-value		Cohen's d
Uric acid (μmol/L) VIF=1.4	1	0.99–1.00	0.03	*	−0.27
Glucosuria (pos vs neg) VIF=1.1	0.42	0.17–1.01	0.052	ns	—
Nitrite (pos vs neg) VIF=1.1	7.23	3.92–13.34	<0.0001	****	—
Creatinine (μmol/L) VIF=1.3	1.01	1.00–1.01	<0.0001	****	0.55
Age (years) VIF=1.3	1.07	1.03–1.11	0	***	0.74
Mean corpuscular volume (fL) VIF=1.3	1.05	1.02–1.08	0.002	**	0.39
MCHC (g/L) VIF=1.5	0.98	0.96–1.00	0.093	ns	−0.31
Model 4: CAD+T2DM+HUA — n = 60 cases/544 total AIC = 345.1 BIC = 375.2 Nagelkerke R^2 = 0.164 Bootstrap AUC = 0.717 [95% CI: 0.620–0.805]					
Predictor (units)	OR per unit	95% CI	p-value		Cohen's d
Nitrite (pos vs neg) VIF=1.1	0.06	0.01–0.48	0.007	**	—
β2-Microglobulin (mg/L) VIF=1.3	0.93	0.82–1.06	0.279	ns	−0.21
Haematocrit (%) VIF=1.4	1.04	1.00–1.09	0.058	ns	0.39
Proteinuria (pos vs neg) VIF=1.1	2.6	1.30–5.19	0.007	**	—
Haematuria (pos vs neg) VIF=1.1	0.41	0.19–0.90	0.025	*	—
Mean corpuscular haemoglobin (pg) VIF=1.1	0.9	0.84–0.96	0.002	**	−0.35
Model 5: CAD+HUA+CKD — n = 54 cases/544 total AIC = 286.0 BIC = 311.8 Nagelkerke R^2 = 0.280 Bootstrap AUC = 0.826 [95% CI: 0.755–0.898]					
Predictor (units)	OR per unit	95% CI	p-value		Cohen's d
Uric acid (μmol/L) VIF=1.1	1	1.00–1.01	0.001	**	0.48
Leukocyte esterase (pos vs neg) VIF=1.0	9.62	4.67–19.79	<0.0001	****	—
β2-Microglobulin (mg/L) VIF=1.1	1.09	0.99–1.20	0.074	ns	0.53
Potassium (mmol/L) VIF=1.1	1.79	1.04–3.10	0.037	*	0.46
Eosinophils ($\times 10^9$/L) VIF=1.0	4.06	1.38–11.90	0.011	*	0.49
Model 6: CAD+T2DM+CKD — n = 17 cases/544 total AIC = 148.2 BIC = 161.1 Nagelkerke R^2 = 0.068 Bootstrap AUC = 0.687 [95% CI: 0.504–0.821]					
Predictor (units)	OR per unit	95% CI	p-value		Cohen's d
Eosinophils ($\times 10^9$/L) VIF=1.0	0	0.00–0.43	0.021	*	−0.49
RDW-SD (fL) VIF=1.0	0.94	0.85–1.03	0.16	ns	−0.28

(*Continued*)

Table 2 (Continued).

Predictor (Units)	OR per Unit	95% CI	*p*-value	Significance	Cohen's d vs Others
Model 7: CAD+T2DM+HUA+CKD — n = 26 cases/544 total AIC = 158.1 BIC = 171.0 Nagelkerke R^2 = 0.311 Bootstrap AUC = 0.873 [95% CI: 0.755–0.959]					
Predictor (units)	OR per unit	95% CI	p-value		Cohen's d
Glucosuria (pos vs neg) VIF=1.0	19.05	6.37–57.04	<0.0001	****	—
Globulin (g/dL) VIF=1.0	0.86	0.78–0.94	0.002	**	−0.75

Notes: Variable selection: Candidate predictors were first restricted to variables surviving FDR correction (Benjamini–Hochberg) across all 27 tested parameters (q < 0.05), yielding 27 candidates. LASSO-penalised logistic regression (10-fold cross-validation, AUROC scoring) was then applied to select the final predictor set for each model. Predictor cap (EPV rule): The maximum number of predictors per model was set to one per 10 events (events-per-variable ≥ 10). Accordingly, models with small case counts (CAD+T2DM+CKD, n = 17; CAD+T2DM+HUA+CKD, n = 26) were limited to 2 predictors. Findings for these two models should be considered exploratory. Reference category: Each binary outcome compares the target subgroup versus all remaining CAD patients combined (n = 544 − n_cases). This heterogeneous reference limits causal inference; ORs reflect discriminability, not absolute risk. OR interpretation: ORs are expressed per one-unit change on the original measurement scale (units shown in parentheses). For binary urinalysis variables (LEU, PRO, GLU, BLD, NIT), OR reflects positive vs. negative dipstick result. Cohen's d: Standardised mean difference between target subgroup and all other patients for continuous predictors. |d| < 0.2 = negligible; 0.2–0.5 = small; 0.5–0.8 = medium; > 0.8 = large (Cohen, 1988). Highlighted values (|d| ≥ 0.5) indicate medium-to-large effects. Model validation: AUC and 95% CIs were estimated by stratified bootstrap resampling (300 iterations, out-of-bag prediction). Bootstrap AUC represents the optimism-corrected estimate; apparent AUC on full data will be slightly higher. Multicollinearity: VIF is reported for each predictor. All selected predictors had VIF < 2.0, indicating negligible multicollinearity. Significance codes: ****p < 0.0001; ***p < 0.001; **p < 0.01; *p < 0.05; ns = p ≥ 0.05. p-values are unadjusted within-model values; variable selection already controlled for multiplicity via LASSO regularisation. Missing data: Analysis used complete cases. No missing values were present for the 27 FDR-significant predictors (N = 544).

and CAD+HUA+CKD (39/54, 72%), whereas CAD+T2DM exhibited a male majority (44/157, 28% male). This aligns with prior reports that CKD prevalence is higher in women, potentially due to hormonal influences and slower progression of early CKD stages compared to men.[16] Similarly, T2DM shows a less pronounced gender disparity in CAD patients, consistent with global epidemiologic data.[17,18] These findings underscore the importance of considering gender in risk stratification and management. Mean age was highest in CAD+HUA (84.7 ± 10.1 years) and lowest in CAD+T2DM+CKD (76.4 ± 11.0 years), with significant differences among subgroups (p=1.77×10^{-7}). This observation is consistent with the German Claims Data-Based Cohort Study, which found that CKD patients were older than those without CKD.[19] Age is a critical determinant of CAD outcomes, as older patients often exhibit reduced physiological reserve and heightened susceptibility to metabolic and renal dysfunction.[20] Future studies should investigate how age-related changes influence disease progression in multi-comorbid CAD populations.

WBC counts were significantly elevated in CAD+T2DM+HUA (8.93 ± 4.09 × 10^9/L) and CAD+CKD (8.31 ± 2.90×10^9/L) compared to CAD+HUA (7.25 ± 3.41 × 10^9/L; p=0.047). Elevated WBC reflects systemic inflammation, a well-established contributor to atherosclerotic plaque instability. Prior studies have shown that combined T2DM and HUA potentiate inflammatory pathways in CAD.[21] These results reinforce the relevance of WBC as an accessible biomarker for cardiovascular risk in complex comorbid populations. RBC counts were lowest in CAD+HUA (3.39 ± 0.90 × 10^9/L), consistent with literature documenting that HUA and CKD contribute to anemia via impaired erythropoiesis and chronic inflammation.[22] Platelet counts were lowest in CAD+T2DM+CKD (199.23 ± 71.42 × 10^9/L), reflecting possible platelet consumption or dysfunction, which has been described in metabolic and renal disorders where uremic toxins and chronic inflammation alter platelet activation and lifespan.[23,24] Leukocyte subset analysis revealed significant elevations in eosinophils in CAD+T2DM+HUA (0.32 ± 0.25 × 10^9/L; p = 0.004), suggesting immune activation pathways beyond neutrophil-mediated inflammation. While lymphocytes and monocytes remained relatively stable, prior studies have linked elevated eosinophil counts with adverse cardiovascular events, particularly in metabolic syndrome.[25] Red cell indices such as MCV, RDW-SD, MCH, and MCHC showed significant differences, highlighting erythrocyte morphological heterogeneity in CKD and metabolic comorbidity. These alterations, often due to iron deficiency, chronic inflammation, or impaired erythropoietin response, have been associated with increased cardiovascular mortality.[22] ALT levels were highest in CAD+CKD (24.45± 26.96 U/L), indicating subclinical hepatic involvement, as previously reported in CKD patients[26] (Hepatology, 2019). Total protein, albumin, and globulin also varied significantly (p<0.01), reflecting chronic inflammation and malnutrition in older and multi-comorbid patients.[27] CRP levels, while not statistically different, showed a trend toward elevation in CKD and multi-comorbid groups, consistent with its role as a marker of cardiovascular risk and systemic inflammation.[28] Electrolytes exhibited significant variation: calcium, sodium,

chloride, and potassium differed across groups, indicative of renal dysfunction and altered metabolic homeostasis. CKD and T2DM patients are prone to dysregulated electrolyte balance due to impaired renal handling and comorbidity-driven metabolic changes.[29,30] Beta-2 microglobulin (BMG) levels were highest in CAD+T2DM+HUA (5.31 ± 2.52 mg/L), supporting its utility as a sensitive marker of renal tubular injury and cardiovascular risk.[31] Urine analysis demonstrated significant differences in SG, pH, and dipstick markers. Positive leukocyte esterase was most frequent in CAD+HUA+CKD (42/12), while proteinuria, glucosuria, and haematuria were higher in CKD and multi-comorbidity groups, consistent with renal impairment and metabolic dysregulation.[32] Interestingly, glucosuria showed an inverse association with the CAD+T2DM+HUA phenotype in the multivariable model. Several explanations may account for this observation. First, glucosuria detected by urine dipstick may reflect transient glycemic fluctuations rather than chronic glycemic exposure.[33] Second, differences in antidiabetic treatment strategies could influence urinary glucose excretion; for example, the use of sodium–glucose cotransporter-2 (SGLT2) inhibitors intentionally increase urinary glucose excretion and may alter dipstick findings independent of glycemic status.[34] Third, patients with better glycemic control or lower plasma glucose levels may be less likely to exhibit glucosuria.[35] Unfortunately, detailed information on HbA1c levels and diabetes medication use was not consistently available in the retrospective dataset. Future studies incorporating longitudinal glycemic measurements and medication profiles are needed to clarify the clinical significance of this association. Elevated urea, creatinine, and uric acid further confirmed renal involvement. These findings reinforce the value of routine urinalysis as a non-invasive tool to detect early renal and metabolic dysfunction in CAD patients.

Multivariate logistic regression identified laboratory predictors of comorbid phenotypes. LEU positivity strongly predicted CAD+HUA+CKD (OR = 6.97, 95% CI 2.61–18.59), glucosuria inversely predicted CAD+T2DM+HUA (OR = 0.21, 95% CI 0.09–0.48), and serum calcium predicted CAD+T2DM+CKD (OR = 6.45, 95% CI 2.70–15.4). These associations highlight the potential for integrating laboratory biomarkers into risk stratification frameworks, as previously recommended in multi-centre cardiovascular studies.[36]

Despite providing detailed characterization, the study is limited by its cross-sectional design, which precludes causal inference. Longitudinal studies are needed to elucidate how laboratory abnormalities progress over time and influence CAD outcomes. Gender-specific interventions should be explored, given observed disparities, especially in CKD. Additionally, integration of emerging biomarkers such as high-sensitivity troponin, NT-proBNP, and advanced imaging could refine risk assessment and enable earlier intervention.[37,38] Future research should also investigate mechanistic pathways linking eosinophilia and inflammatory markers with atherosclerotic progression in metabolically complex patients. The retrospective design may introduce selection bias, and reliance on electronic health records limits access to lifestyle, socioeconomic, and medication adherence data. Because the regression analyses were performed within a single-center retrospective dataset, there is a possibility of model overfitting, particularly when multiple laboratory variables are included in multivariable models. Although variables were selected based on clinical relevance and statistical significance to reduce unnecessary model complexity, formal internal validation techniques such as cross-validation or bootstrapping were not applied. Therefore, the predictive associations identified in this study should be interpreted with caution. Future studies involving larger multi-center cohorts with internal validation procedures and independent external validation are necessary to confirm the robustness, reproducibility, and generalizability of these findings. Nonetheless, the study provides a robust, multi-dimensional characterization of CAD patients with common comorbidities, offering clinically actionable insights for risk stratification and management.

Conclusion

This study demonstrates that haematological, biochemical, and urinary biomarker profiles differ across coronary artery disease phenotypes defined by metabolic and renal comorbidities. These findings highlight the potential value of integrating multi-compartment laboratory indicators to better characterize heterogeneity in CAD patients. However, given the retrospective single-centre design and exploratory analyses, the observed associations should be interpreted cautiously. Further validation in larger, independent prospective cohorts is required to determine whether such biomarker patterns may inform future risk stratification approaches.

Ethical Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Institutional Ethical Committee of Guangzhou Liwan Central Hospital, Guangzhou, China (Approval Number: 2025024).

As this was a retrospective study using de-identified patient data, the requirement for individual informed consent was waived by the committee.

Consent for Publication

Not applicable as no individual patient data or identifiable images are included in this manuscript.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest relevant to this work.

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